Remarks

Original claims 82-90, 94-96 and 100-102 as now amended and new claims 130-147 will be pending after entry of this amendment; these claims are directed to methods to treat hepatitis C virus in a host using various 1', 2' or 3'-branched nucleosides. New claims 130-140 are directed to methods to treat HCV using branched nucleosides with pharmaceutically acceptable carriers. Support for these claims can be found on page 55, line 13 to page 57, line 33 of the specification. New claims 141-147 are specifically directed to methods to treat humans, which find support on page 50, lines 25-26.

Enclosed hereto is a marked up version of the changes made by the current amendment, in accordance with 37 CFR §1.121 (c). The enclosed page is captioned "**Version with Markings to Show Changes Made**."

The Examiner has restricted the prosecution of the present application to one of two groups of claims. Group I consists of original claims 1-51 and 79-102, drawn to compounds, compositions and methods of using such compounds. Group II consists of original claims 52-78 and 103-129, drawn to compositions comprising such compounds in combination with one or more other antivirally effective agents, and methods of using such compositions. In addition, the Examiner has requested that the Applicants select a species to initiate prosecution. Species A is directed to compounds, compositions and methods drawn to pyrimidine nucleosides. Species B is directed to compounds, compositions and methods drawn to purine nucleosides.

Applicants elect claims 82-90, 94-96 and 100-102, as defined in Group I, Species A, and have added new claims 130-147. This election is made without traverse.

Respectfully submitted,

Sherry M. Knowles, Esq.
Registration No. 33,052

By Express Permission
Reg. No. 48,308

Date: August 15, 2002

Enclosure: Version with Markings to Show Changes Made

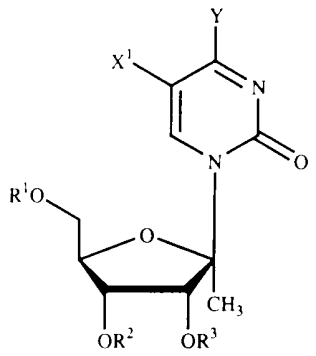
King & Spalding
191 Peachtree Street
Atlanta, Georgia 30303
Telephone: 404-572-3541
Facsimile: 404-572-51305

Version with Markings to Show Changes Made

In the Claims

Claims 82-90, 94-96 and 100-102 were amended as follows:

82. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula IV:



(IV)

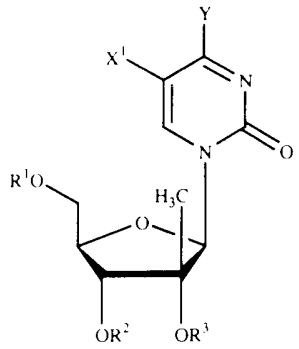
or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl [~~(including lower acyl)~~] or alkyl [~~(including but not limited to methyl, ethyl, propyl and cyclopropyl)~~].

83. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula V:



(V)

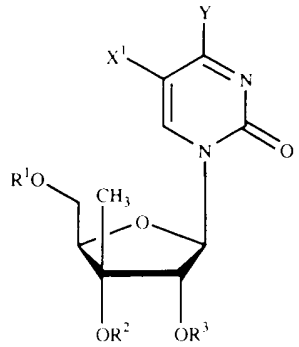
or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl [~~(including lower acyl)~~] or alkyl [~~(including but not limited to methyl, ethyl, propyl and cyclopropyl)~~].

84. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VI:



(VI)

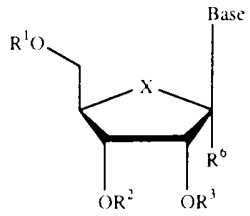
or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or

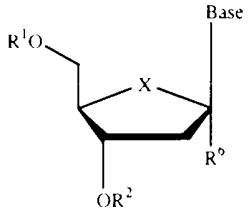
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl [~~(including lower acyl)~~] or alkyl [~~(including but not limited to methyl, ethyl, propyl and cyclopropyl)~~].

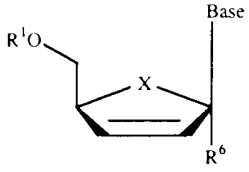
85. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VII, VIII or IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a [~~purine or~~] pyrimidine base [~~as defined herein~~];

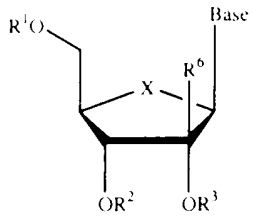
R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is [hydrogen,] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl,

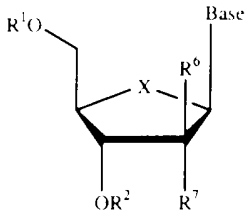
NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH

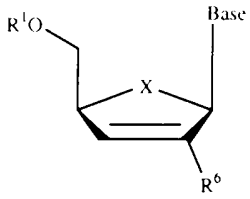
86. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula X, XI or XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a [~~purine or~~] pyrimidine base [~~as defined herein~~];

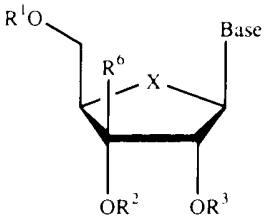
R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is [~~hydrogen,~~] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~] -O(alkyl), [~~-O(lower alkyl),~~] -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

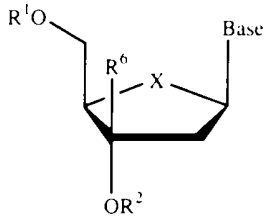
R^7 is [~~hydrogen,~~] OR^3, hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~]

X is O, S, SO$_2$ or CH$_2$

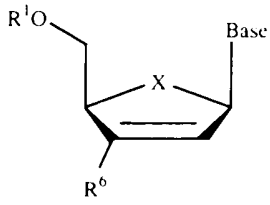
87. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XIII, XIV or XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, wherein:

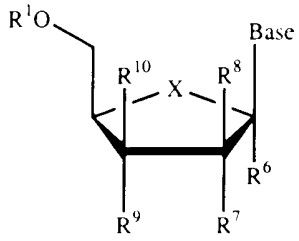
Base is a [~~purine or~~] pyrimidine base [~~as defined herein~~];

R^1, R^2 and R^3 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is [~~hydrogen,~~] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~] -O(alkyl), [~~-O(lower alkyl),~~] -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

88. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a [~~purine or~~] pyrimidine base [~~as defined herein~~];

R^1 and R^2 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is [~~hydrogen,~~] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~] -O(alkyl), [~~-O(lower alkyl),~~] -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

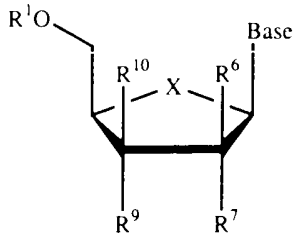
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl),

R^8 and R^{10} are independently H, alkyl, [~~including lower alkyl~~], chloride, bromide or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

89. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a [~~purine or~~] pyrimidine base [~~as defined herein~~];

R^1 and R^2 are independently H; [~~, phosphate (including~~] mono-, di- or triphosphate; [~~and~~] a stabilized phosphate [~~prodrug)~~]; acyl [~~(including lower acyl)~~]; alkyl [~~(including lower alkyl)~~]; sulfonate ester; [~~including~~] alkyl or arylalkyl sulfonyl; [~~including~~] methanesulfonyl; [~~and~~] benzyl, wherein the phenyl group is optionally substituted with one or more substituents [~~as described in the definition of aryl given herein~~]; a lipid; [~~including~~] a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is [~~hydrogen,~~] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~] -O(alkyl),

... is [and R ... are independently hydrogen, [OR ... hydroxy, alkyl [including lower alkyl], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl),

R^6 is [~~hydrogen,~~] hydroxy, alkyl [~~(including lower alkyl)~~], azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), [~~-C(O)O(lower alkyl),~~] -O(acyl), [~~-O(lower acyl),~~] -O(alkyl), [~~-O(lower alkyl),~~] -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 **is** [~~and R^9 are independently~~] hydrogen, OR^2, alkyl [~~(including lower alkyl)~~], alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

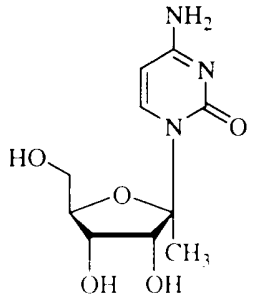
R^9 is OR^2, alkyl, alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl [~~(including lower alkyl)~~], chlorine, bromine or iodine;

[~~alternatively, R^7 and R^9 and R^8 and R^9 can come together to form a bond;~~] and

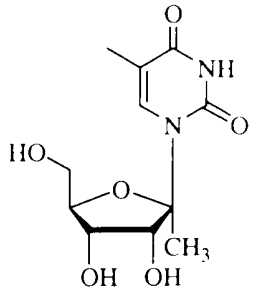
X is O, S, SO_2 or CH_2.

94. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



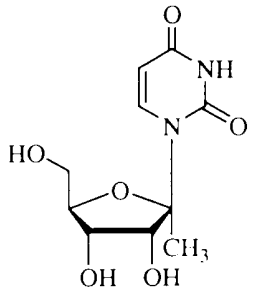
or a pharmaceutically acceptable salt thereof.

95. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



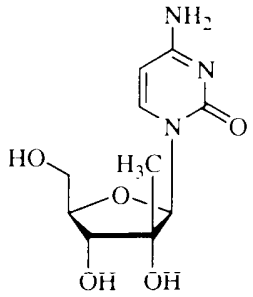
or a pharmaceutically acceptable salt thereof.

96. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



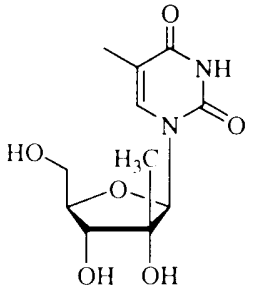
or a pharmaceutically acceptable salt thereof.

100. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



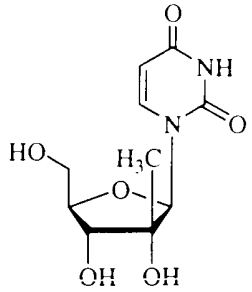
or a pharmaceutically acceptable salt thereof.

101. (Once Amended, Marked Up) A method for the treatment [~~or prophylaxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt thereof.

102. (Once Amended, Marked Up) A method for the treatment [~~or prophyluxis~~] of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt thereof.